## REMARKS

Applicants re-affirm the election of Group I, claims 32-40 and 50; and re-affirm the election for examination the species where:

(1) the compound having vitamin PP activity or prodrug thereof is nicotinamide, a compound [*see* claim 32, for example] of formula V where b is 1, and $R^{21}$, $R^{22}$, $R^{23}$, $R^{26}$, and $R^{27}$ are all hydrogen; and

(2) the compound of formula I is N-[4-(1-benzoylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, a compound [*see* claim 38, for example] where each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ is hydrogen, k is 0, $A^{(i)}$ is -CH=CH-, $D^{(i)}$ is $-(CH_2)_4-$, E is piperidin-4-yl, and G is 1-benzoyl.

Claims readable on the elected species are claims 32-36, 38-40, 50, 53, and 54.

Entry of this amendment is respectfully requested. No new matter is added by the amendment because the amended claims and the newly added claims are fully supported by the application as filed.

Claims 32-56 are in this application; no claims having been cancelled; claims 33, 35, 41, 46, 50 and 52 having been amended, and claims 53-56 having been added by this amendment.

The amendments was made to:

(1) clarify the terms "thioxo analogs" or "thioxo derivatives" to mean the replacement of the C=O groups with the corresponding C=S analogs in Claims 32, 33, 35, 41, and 46;

(2) clarify the phrase "such that the alcohol $R^{25}(OH)_a$" to clearly define that $R^{25}$ is the residue of the alcohol $R^{25}(OH)_a$ in Claims 33 and 41;

(3) replace the terms "anionic salts" with the terms "pharmaceutical acceptable salts" in Claim 33, 35, 41 and 46;

(4) delete the phrase "acid addition salts" as the phrase "pharmaceutical acceptable salts" encompasses acid addition salts (page 49, first line) in Claims 33 and 41; and

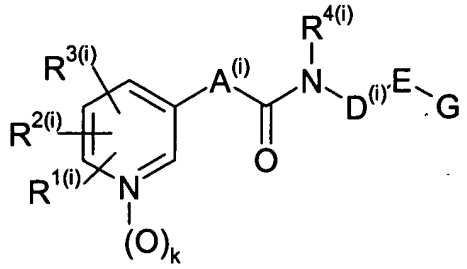
(5) correct minor typographical errors or additions in Claims 45, 50 and 52.

In the Office Action mailed June 9, 2003, the Examiner maintained the restriction requirement between Groups I - IV; and Applicants respectfully traverse the restriction requirement based on the same reasoning put forth in Applicants' response of February 6, 2003.

Namely, the compounds having vitamin PP activity of Group II are simply heterocyclyl ethers of the compounds of formulae (II), (IIa), and (IIb) where the homocyclyl ethers are classified in Group I, and the compounds of Group III are simply sugar ethers of the compounds of formulae (II), (IIa), and (IIb) where the non-sugar ethers are classified in Group I [and yet the sugars are simply a special case of the "tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms" of claim 33]. Further, claims 32 and 33 at least are linking claims with respect to the compounds having vitamin PP activity. In addition, the compound having vitamin PP activity is defined both generically in claim 32 and subgenerically by the Markush group in claim 33; and the compound of formula I is defined by Markush group in claim 38.

Furthermore, the compounds having vitamin PP activity clearly share a common utility (the vitamin PP activity itself), and share a substantial common feature disclosed as being essential to that activity (all the compounds are based on a 3-pyridyl nucleus and are 3-pyridylmethanols or their ethers, 3-pyridylcarboxylates [nicotinic acids], or 3-pyridylcarboxamides [nicotinamides], and their N-oxide or quaternary ammonium derivatives).

Applicants also note that the compounds of formula I also share a common activity (they are disclosed as cancerostatic or immunosuppressive agents), and share a substantial common feature disclosed as being essential to that activity (all the compounds are of the formula



(I)

as defined in claim 38.

With respect to the restriction requirement between Groups I - IV and V, method claims and composition claims, Applicants respectfully submit that the compositions of Group V are linked to the method claims by their activity, and respectfully request that, should the method claims be narrowed during examination so that there will be composition claims of a compound scope as great as the scope of the then-examined method claims, that composition claims then be examined with method claims since the search for the compositions and methods is likely to be co-extensive so that no additional effort on the part of the Office will be required.

The Examiner rejected Claim 33 under 35 U.S.C. 112, first paragraph, as containing subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention because the Examiner alleges that the recitation within the definition of $R^{27}$ "in which a methylene group is optionally replaced by O, NH or N-alkyl" does not disclose the site at which the replacement occurs, and that the terminal $R^{27}$ cannot be O or NH.

First, it is common sense to one skilled in the art of organic synthesis that: a) alkylene groups having a methylene group can be readily replaced with a heteroatom such as O, NH or N-alkyl. For example, for an alkylene linker such as X-$CH_2$-$CH_2$-$CH_2$-$CH_2$-Y, one -$CH_2$- can be readily replaced isosterically with a hetero atom such as O, NH or the group N-alkyl in any desired position where the replacement is synthetically

feasible based on the available starting materials, and that the isosteric replacement of the above hetero atom adjacent to a group such as -C(O)-N($R^{26}$)- to form a -C(O)-N($R^{26}$)-O-, -C(O)-N($R^{26}$)-NH- or an -C(O)-N($R^{26}$)-N-alkyl group, while synthetically feasible for certain compounds, may not occur as readily with all possible derivatives. And b) in Claim 33, when b is 2, then $R^{27}$ is not a terminal group, and therefore, $R^{27}$ can be O or NH.

The Examiner rejected Claims 32-36 under 35 U.S.C. 102(a) as being anticipated by Budihardjo et al because the Examiner alleges that Budihardjo teaches the therapeutic administration of the nicotinamide derivative, 6-aminonicotinamide, which can be metabolized in vivo to a compound with vitamin PP activity.

Claim 32 in the present application claims a "method for preventing, reducing, or eliminating side effect or neutralizing the side effects of a cancerostatic or immunosuppressive agent" while Budihardjo teaches that 6-aminonicotinamide (6AN) increases the sensitivity of human cancer cells to cisplatin. See Budihardjo, p. 122, 2nd column. Budihadjo does not teach nor suggest the use of any agent to protect non-tumor cells, which is an important aspect of reducing the side effects of cancerostatic or immunosuppressive agents such as cisplatin therapy as taught in the present invention.

The Examiner rejected Claims 32-36 under 35 U.S.C. 102(b) as being anticipated by Artemov, V.A. However, Artemov teaches that pyridoxine negates the immunodepressive effect of 6-mercaptopurine when given in optimal doses, which suggests that the method reduces the immunodepressive effect of an immunodepressant, but the study does not show or suggest any methods for preventing, reducing or eliminating the side effects caused by the agent.

New Claims 53 and 54 have been added to the elected subject matter and covers a limited number of vitamin PP compounds wherein the compounds encompass derivatives that exclude morpholinyl derivatives in group E, and further limits group G to a Markush group of ring systems having no heteroatoms. New Claims 55 and 56 have been added to encompasss the same subject matter as in new Claims 53 and 54 and

specifically claims "the sodium, potassium, magnesium, calcium or aluminum salts thereof." Support for the specific salts are found at the bottom of page 55.

Entry of the amendment and allowance of the claims are requested.

Respectfully submitted,

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